REMARKS/ARGUMENTS

Claims 1, 9, 18, 19, 105-108 and 114-117 are active in this case.

The claims have been amended to change the sequence identifier to SEQ ID NO:38 in Claims 1 and 105 and to add further embodiments of human G-CSF as in SEQ ID NO:37 and 39. Support for these changes is found on pages 22-23 of the application as originally filed. The sequence listing provides support for these sequences as well.

No new matter is added.

Applicants thank the Examiner for the courtesy of meeting with their undersigned representative on September 14, 2009 to discuss the issues presented in the Action.

During this meeting, the written description rejection was discussed.

It was again explained that G-CSF is a well-known factor as described throughout the specification as previously discussed. In addition, reference was made to the publication of Aritomi et al (*Nature* 401:713-717 (1999), copy previously provided), which shows that before the present application was filed the structure of the G-CSF and its relationship with its receptor was well-known.

In addition, three additional publications are attached here demonstrating that at the time of filing, the structure function relationship was known for G-CSF (see Hill et al *Proc Natl Acad Sci, USA*, vol. 90, 5167-5171 (1993); Layton et al *J Biol Chem* 266(35):23815-23823 (1991); and Filgrastim in Clinical Practice, 2nd edition, Chapter 2, Morstyn et al (Ed.), Marcel Dekker, Inc. (1998)).

Thus, which amino acids can be modified is well-within the knowledge in the art as also set forth in the specification (see page 20, second paragraph to page 22, first paragraph). The fact that G-CSF has a known structure and that it was known what portions of that structure correlate to its function plus the disclosure of numerous species in the application and known in the art demonstrates that the claims satisfy the written description requirement

(see *Capon v. Eshhar* (Fed. Cir. 2005): "When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh."; see also *Falkner v. Inglis,* 79 USPQ2d 1001 (Fed. Cir. 2006): "Recitation of Known Structure Is Not Required" to satisfy written description requirement).

Reconsideration and withdrawal of the rejection is requested.

The discussion then turned to the rejections citing the newly cited Whalen et al publication (Crit Care Med 28(11) Nov. 2000).

Whalen examines various neurological parameters (such as BBB damage, brain edema, or brain neutrophil accumulation) after traumatic brain injury (TBI) with a prior administration of G-CSF or vinblastin. Therefore, Whalen teaches administrating GCSF before TBI, which is not the same as administering G-CSF to a mammal suffering from TBI, that is, the administration of G-CSF occurs after the injury in the claims whereas in Whalen the G-CSF is administered before injury.

More specifically, Whalen at page 3711 describes three protocols in the "Experimental Groups" (2nd col.). In each of those protocols, it is clear that G-CSF is administered before the injury causing TBI and 24 hours after the injury, the various indicia were assessed. Notably, this is summarized quite clearly in Whalen's Abstract:

> Protocol I . . . rats . . . receive . . . GCSF to increase ANC, or saline before controlled cortical impact. . ."

> "Protocol III: rats received GCSF or saline before CCI."

> "Protocol III: rats received GCSF or saline before CCI."

Therefore, the prior administration of G-CSF to modulate physiologic parameters prior to the injury is completely different to the therapy of existing TBI by G-CSF administration as claimed.

Therefore, the claims are not anticipated by this disclosure.

Additionally, Whalen found that all parameters observed after TBI are either unchanged (brain edema and brain neutrophil accumulation) or became worse (BBB damage). Again, see, e.g., the Abstract: "Increasing systemic ANC before CCI with GCSF administration does not increase post-traumatic brain neutrophil accumulation or brain edema after CCI in rats." Therefore, one would not be motivated based on Whalen to treat a subject suffering from TBI with GCSF, particularly as Whalen's results were overall negative to the idea of using G-CSF.

Withdrawal of the rejection citing Whalen is requested.

For similar reasons, the claims would not have been obvious in view of Whalen with (A) Brines; (B) Deleuze; (C) Morita-Fukimura; and (D) Neupogen® product information as alleged in the separate rejections applied under 35 USC 103(a).

Claims 5-7 have been cancelled thus the rejection combining Brines and Whalen is not applicable. Further, Brines is relied upon to treat a combination treatment of TBI with erythropoietin (as an example of an additional hematopoietic factor). However, as Whalen does not teach treating TBI in the manner that is claimed one would not have found guidance in Brines to supplement Whalen's protocol nor would one have incentive to do so given Whalen's negative report of success with G-CSF.

Claim 12 has been cancelled and thus the rejection combining Deleuze and Whalen is not applicable. Further, Deleuze is relied upon to treat a combination treatment of TBI with TPA. However, as Whalen does not teach treating TBI in the manner that is claimed one would not have found guidance in Deleuze to supplement Whalen's protocol nor would one have incentive to do so given Whalen's negative report of success with G-CSF.

Claim 14 is cancelled and as such the rejection combining Morita-Fujimura is not applicable. Further, Morita-Fujimura is relied upon to treat a combination treatment of TBI with caspase inhibitors. However, as Whalen does not teach treating TBI in the manner that is claimed one would not have found guidance in Morita-Fujimura to supplement Whalen's protocol nor would one have incentive to do so given Whalen's negative report of success with G-CSF.

The rejection combining Neupogen® and Whalen is not applicable. Neupogen® is relied upon to teach intravenous administration. As Whalen does not teach treating TBI in the manner that is claimed one would not have found guidance in Neupogen® to supplement Whalen's protocol nor would one have incentive to do so given Whalen's negative report of success with G-CSF.

Reconsideration and withdrawal of all of the obviousness rejections applied under 35 USC 103(a) is requested.

A Notice of Allowance is also requested.

Respectfully submitted,

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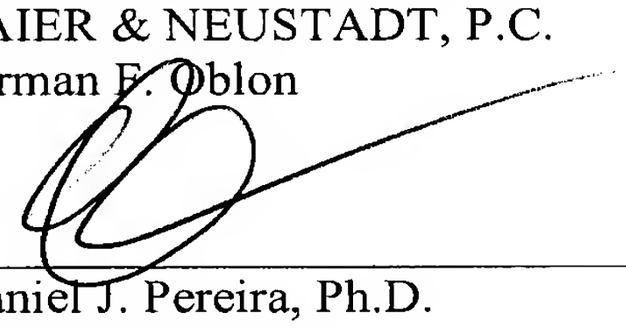
Norman F. Oblon



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